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EXAMINER	
PALENIK, JEFFREY T	

ART UNIT	PAPER NUMBER
1615	

NOTIFICATION DATE	DELIVERY MODE
12/10/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/523,012	MOORMANN ET AL.	
	Examiner	Art Unit	
	Jeffrey T. Palenik	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8-16 and 18-22* is/are pending in the application.

4a) Of the above claim(s) *10-16,18,19 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8,9,20 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of Applicants' Amendments and Remarks filed 18 July 2008. The Examiner acknowledges the following:

New claims 20-22 have been added. Claims 7 and 17 have been cancelled.

Claims 10-19 which were previously only withdrawn from consideration currently remain so. New claim 22 is presently also withdrawn from consideration since it depends from claim 12.

Though amendments have been made to all pending claims, the claims presently under consideration, only claims 1-6, 8 and 9 are addressed here. Where support for the amendments was not expressly provided, it was found either within Applicants' disclosure and/or originally filed claims. The Examiner acknowledges that no new matter has been added to the claims.

Thus, claims 1-6, 8, 20 and 21 now represent all claims currently under consideration.

PRIORITY

Applicants' continuity of priority has been verified via the documents previously submitted. The Examiner thanks Applicants for pointing out the incorrectly applied time requirement. However, Applicants are still denied priority to DE 102 35 556.8, filed 3 August 2002, since no distinguishable English translation of the Foreign Application has been submitted. Per MPEP §1893.01(d), an English translation of the international application is required when entering the national stage in the U.S. Applicants' response indicates that such a translation was submitted. However, after examining each document submitted by

Applicant on 9 June 2008, the Examiner respectfully submits that an English translation cannot be discerned. Otherwise stated, there were no submissions by Applicants indicating either a certified translation of the foreign application or any documents (i.e. Specification, claims, etc.) demonstrating clear and unswerving continuity back to the foreign application. Until such time as this is provided, Applicants' effective U.S. filing date will remain 25 July 2003.

INFORMATION DISCLOSURE STATEMENT

No new Information Disclosure Statement (IDS) have been submitted for consideration.

WITHDRAWN OBJECTIONS/REJECTIONS

Objection to the Specification

Applicants' remarks regarding both the Abstract and Title of the Invention render moot their objection. Thus, after fully considering Applicants' remarks, said objections have been **withdrawn**.

Rejection under 35 USC 112

Applicants' amendments removing the "can be" limitations from claims 1 and 9, removing the "preferred" limitation from claim 2, and clarifying the language regarding the administration forms in claim 8, render moot the rejections to claims 1, 2, 8 and 9, under 35 USC 112, second paragraph. Thus, said rejections have been **withdrawn**.

Rejection under 35 USC 102(b)

Applicants' amendments to the instant claims, namely claim 1, render moot the rejection to claims 1-3, 5 and 6, under 35 USC 102(b) as being anticipated by McGee et al. (USPN 7,160,559 or WO 2000/38686). Thus, said rejection has been **withdrawn**.

Rejection under 35 USC 103(a)

Applicants' amendments to the instant claims, namely claim 1, render moot the rejection to claims 1-6, 8 and 9 under 35 USC 103(a) as being unpatentable over McGee et al. in view of Plata-Salaman et al. (US Pre-Grant Publication N° 2003/0060423). Thus, said rejection has been **withdrawn**.

NEW REJECTIONS

In light of Applicants' amendments, most notably to claims 1 and 9, as well as the addition of new claims 20 and 21, the following rejections have been newly added:

CLAIM REJECTIONS - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 recites that the rapid-entry form of the dose "*is capable of being* sprayed or dripped into the nose" [emphasis added]. Despite Applicants' amendment to the claim, it remains unclear, whether this limitation is part of the invention, since application of a liquid formulation by way of a nozzle does not necessitate pernasal spraying or dripping.

CLAIM REJECTIONS - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the

time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6, 8, 9, 20 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Biberman (US Pre-Grant Publication N° 2002/0019421) in view of Plata-Salaman (US Pre-Grant Publication N° 2003/0060423).

The instantly amended claims are directed to a composition consisting of two administration forms: 1.) an administration form that continuously releases at least one modulator of nicotinic receptors and 2.) an administration form which enables a rapid entry of galanthamine or one of its salts in to the Central Nervous System, wherein the second form is now further limited to one of the following routes of administration: buccal (i.e. sublingual) solutions, spray solutions or drip solutions (claim 1). The dependent claim 2 further limits the modulator of nicotinic receptors in the continuous release form to galanthamine, nicotine, or their respective pharmaceutically acceptable salts. The dependent claim 3 further limits the continuous release administration form to transdermal therapeutic systems, subcutaneous implants or intramuscularly injectible preparations. Claim 4 further limits the composition of claim 3 such that the intramuscularly injectible preparation is a suspension of microcapsules containing the modulator(s). Claim 5 further limits the continuous release administration form to either release between 10 and 25 mg of galanthamine or a pharmaceutically acceptable salt of it, or between 5 and 50 mg of nicotine or a pharmaceutically acceptable salt of it. The dependent claim 6 further limits the quick entry administration form of the composition such that it contains 1 to 5 mg of galanthamine or a pharmaceutically acceptable salt of it. Claim 8 has been amended to further limit claim 1 such that the administration

format for the rapid entry form is a flexible plastic container having a capacity between 1-5 mL. Claim 9 further limits claim 8 such that said plastic container is provided with nozzles through which the solution can be sprayed or dripped intranasally. New claim 20 further limits claim 1 such that the two dosage forms are administered independently. Claim 21 further limits the modulator of nicotinic receptors of claim 2 such that the modulator is galanthamine.

Biberman teaches a pharmaceutical composition comprising an amount of an inhibitor of monoamine oxidase (MAOI), an amount of an addictive substance and a suitable carrier (claim 1). Claims 29 and 30 teach the combination of the two aforementioned drug types wherein the addictive substance is nicotine and wherein the composition further comprises at least one additional compound such as an inhibitor of acetylcholine esterase or a nicotine antagonist, an example of which is galanthamine hydrobromide ¶¶[0071] and [0072]. Paragraph [0072] further teaches that both the MAO inhibitor and the addictive substance may be combined where desired with said additional compound. Paragraph [0094] expressly teaches nicotine and an MAO inhibitor such as selegiline as being co-administered via different routes (i.e. orally dosed selegiline and transdermally administered nicotine). Liquid forms of the active compounds are taught as being administered in the form of sterile injectable suspensions or aerosols ¶¶[0080] and [0113]. Additional carrier forms which may be used to administer both the addictive substance and MAO inhibitor are taught as including parenteral forms (i.e. transdermal, subcutaneous, and intramuscular) as well as sublingual (i.e. buccal) and respiratory mucosal (i.e. nasally) forms (claim 18). Paragraph [0078] teaches the

limitations of claim 5 wherein nicotine is co-administered 1-6 times a day ranging from 0.7 to 70 mg per dose.

Biberman does not expressly teach the rapid-release entry form as containing 1-5 mg of galanthamine (claim 6), that the rapid entry release form is administered via a flexible plastic container having a nozzle and volume between 1-5 mL, or that the modulator of nicotinic receptors is solely galanthamine (claim 21).

The teachings of Plata-Salaman, discussed in the previous correspondence, have been included here for Applicants' convenience.

Plata-Salaman teaches co-therapy compositions comprising a therapeutically effective amount of one or more acetylcholinesterase inhibitors ¶¶[0018] and [0071] such as galanthamine ¶[0055]. Administration of galanthamine is taught to range from about 2 to about 32 mg daily and more preferably from about 4 to about 24 mg once or twice daily ¶[0070]. The term "co-therapy," as defined in ¶[0033], refers to at least one compound of a general "formula I" being administered with at least one acetylcholinesterase inhibitor wherein said compound(s) and inhibitor(s) are administered simultaneously, sequentially, separately or in a single pharmaceutical formulation. Instances where dosing does not occur in a single formulation, the routes of administration may be varied and include: intramuscular, transdermal, subcutaneous, as well as being directly applied to the nervous system. Topical, intranasal administration of the active agent is also taught ¶[0076]. Unit dose forms such as tablets, pills, and capsules, each of which include immediate-, timed-, and sustained release formats, are taught ¶ [0072]. Additional dosing systems and formats such as injected (e.g.

parenteral) suspensions, metered liquid sprays, drops, ampoules, and autoinjector devices are taught [0072], each of whose design is capable of incorporating distribution nozzles.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare a medicament consisting of two independent, but concurrently administered dosage forms, wherein one or both of said forms comprises galanthamine as taught by Biberman and as suggested by the combination of Biberman and Plata-Salaman, modify the rapid-release dosing form, and produce the instantly claimed composition.

One of ordinary skill in the art would have been motivated to do this because, as discussed above, both Biberman and Plata-Salaman expressly teach therapeutic regimens which comprise co-administration of dosage forms both of which further comprise galanthamine. Both Biberman [0094] and Plata-Salaman [0033] clearly overlap in their teachings of different routes of administration, and thus inherently teach different rates of delivery (i.e. immediate- versus sustained-release). Both co-administration inventions are also directed towards treating addiction-linked addictions. Biberman is primarily directed to treating addictions to alcohol and smoking as well as secondarily treating various forms of nervous disorders such as dementia, Alzheimer's disease and Parkinson's disease ¶[0060]. Plata-Salaman, on the other hand is conversely directed towards treating primarily treating neurological disorders such as the aforementioned and secondarily directed to treating addictions such as alcoholism as it relates to neurological disorders (claim 10). Regarding the instantly claimed rapid-release entry form, both of the inventions to Biberman ¶[0080] and Plata-Salaman ¶[0075] again overlap in their teachings that dosages may be provided in

sterile, liquid suspension format via injection. Their application nasally is also discussed above. Furthermore, as discussed in the previous correspondence, the skilled artisan would have been motivated, with minimal undue experimentation, to create the necessary result-effective modifications to enable a nozzle-endowed, dosing format to release 1-5 mL of the galanthamine composition through adjustment of manufacturing parameters of said format and reasonably would have expected success because the prior art dealt with the same subject matter of co-therapy, immediate- and sustained-release of a galanthamine formulation. Thus, absent some demonstration of unexpected results from the claimed parameters, optimization of the rapid-release dosage container would have been obvious at the time of Applicants' invention.

Since both of the inventions to Biberman and Plata-Salaman overlap in their teachings, as discussed above, one of ordinary skill in the art would have been particularly motivated to prepare the instantly claimed dual-route administration form. Thus, it would have been *prima facie* obvious to combine the teachings, each of which are taught by the art as being useful for the same purpose, in order to form a third composition, such as that which is instantly claimed, to be used for the very same purpose; the idea of combining them flowing logically from their having been individually taught in the prior art (MPEP §2144.06). In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980)

From the teachings of the reference, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art

at the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

All claims have been rejected; no claims are allowed.

CONCLUSION

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

CORRESPONDENCE

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey T. Palenik whose telephone number is (571) 270-1966. The examiner can normally be reached on 7:30 am - 5:00 pm; M-F (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jeffrey T. Palenik/
Examiner, Art Unit 1615

/MP WOODWARD/
Supervisory Patent Examiner, Art Unit 1615